

MSRHTC

P.O. Box 6507
Aurora, CO 80045-0507
(303) 724-0724



Stroke in Children and Young Adults



**An Overview for Patients and
Health Care Providers**

Awareness • Prevention • Treatment • Support

GLOSSARY:

ischemic stroke = an event or process leading to brain tissue injury, caused by too little blood flow and/or supply of oxygen and other nutrients to the brain

thrombophilia = a condition of increased risk for developing blood clots in the veins or arteries due to increased blood clotting

perinatal/neonatal stroke = stroke occurring around the time of birth or within approximately the first month of life (the most common time for stroke in children), often suspected due to seizure or other neurologic abnormalities

metabolic disorder = a broad category of medical conditions caused by abnormalities in proteins called “enzymes” that control levels of important chemicals and nutrients in the blood or body tissues

thromboembolic stroke = a type of ischemic stroke (see definition above) due to blood clots that have traveled to the brain circulation, often suspected when more than one area of new stroke is seen on brain scans, or in patients with thrombophilia (see definition above)

antiphospholipid antibody syndrome = a type of thrombophilia (see definition above) due to proteins, called “antiphospholipid antibodies,” that are consistently present in the blood over time following a stroke or blood clot in the vein, or in some women who have a history of miscarriage(s)

rheumatologic condition = a broad category of medical disorders (including lupus, juvenile rheumatoid arthritis, and others) in which the body’s immune system is overactive, and sometimes found to be the cause of antiphospholipid antibody syndrome or inflammation of the arteries in the brain in young patients with stroke

This educational overview focuses on ischemic stroke in children and young adults who do not have sickle cell disease. Patients who have sickle cell disease should contact their physician for appropriate educational materials specifically for sickle cell disease.

AUTHOR:

Neil A. Goldenberg, MD

*Department of Pediatrics, Center for Cancer and Blood Disorders
Department of Medicine, Division of Hematology/Oncology
University of Colorado at Denver and Health Sciences Center
The Children's Hospital, Denver, and
The Mountain States Regional Hemophilia and Thrombosis
Center, Aurora, CO*

ACKNOWLEDGEMENT:

Review of manuscript:

Marilyn Manco-Johnson, MD, Denver/Aurora, CO

Timothy Bernard, MD, St. Paul, MN

Stephan Moll, MD, Chapel Hill, NC

Brenda Riske, MBA/MPA, Denver/Aurora, CO

Layout:

Jeff Brazee, Denver/Aurora, CO

SELECTED REFERENCES

“Antithrombotic therapy in children: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy”. Monagle P et al. *Chest* 2004;126:645S-687S.

“Stroke in childhood: clinical guidelines for diagnosis, management and rehabilitation, 2004.” Pediatric Stroke Working Group.

<http://www.rcplondon.ac.uk/pubs/books/childstroke> (accessed 10/11/2006)

“Report of the National Institute of Neurological Disorders and Stroke Workshop on Perinatal and Childhood Stroke.” Lynch JK et al. *Pediatrics* 2002;109:116-123.

“Laboratory testing for thrombophilia in pediatric patients. On behalf of the Subcommittee for Perinatal and Pediatric Thrombosis of the Scientific and Standardization Committee of the International Society of Thrombosis and Haemostasis (ISTH)”. Manco-Johnson J et al. *Thromb Haemost* 2003;89:204-5.

WHAT IS ISCHEMIC STROKE?

There are two major types of stroke: *hemorrhagic* (stroke due to bleeding) and *ischemic*. *Ischemic stroke* is an event or process leading to brain tissue injury, caused by too little blood flow and/or supply of oxygen and other nutrients to the brain.

Stroke in elderly adults is typically due to high blood pressure, atherosclerosis (“hardening of the arteries”), heart arrhythmias, and/or other diseases that affect blood vessels, sometimes in combination. In children and young adults, stroke can be caused by abnormalities in blood vessels in the brain or neck, thrombophilia (excess clotting) states, sickle cell disease, and certain heart or metabolic conditions. Often, however, the cause of stroke in young people remains unclear. This is especially true for stroke occurring in the perinatal/neonatal period (stroke diagnosed in an infant following the development of seizure or other neurologic signs/symptoms anytime within the first few minutes to approximately one month after birth) – the most common time for stroke in childhood.

WHY IS ISCHEMIC STROKE IMPORTANT IN CHILDREN AND YOUNG ADULTS?

Ischemic arterial stroke in children and young adults occurs less commonly than in elderly

adults, but its consequences can be equally devastating. In particular, issues of evaluation for causes and risk factors, short-term stroke treatments, rehabilitation, and long-term prevention of future strokes all play a very prominent role in stroke care for children and young adults. In addition, because stroke is a rare disorder in children and young adults, optimal stroke care in young people requires expertise from a variety of medical specialties, including blood clotting, neurology, radiology, rehabilitation (“rehab”), neuropsychology, and other areas. Although some guidelines have been proposed for the evaluation and treatment of stroke in children and young adults, the particular circumstances of each patient must also be considered. This highlights the importance of expertise in stroke care for young people, and is also important to keep in mind when reading this general overview.

HOW IS ISCHEMIC STROKE DIAGNOSED IN CHILDREN AND YOUNG ADULTS?

Ischemic stroke in young people may occur with a variety of signs and symptoms, depending mainly on the area of the brain that is affected. These signs and symptoms can include: new-onset seizure; one-sided weakness or numbness; facial droop; slurred speech; sudden change in vision; difficulties with walking, balance, or coordination; or unexplained change in level of consciousness.

KEY SUMMARY POINTS

- Ischemic arterial stroke in children and young adults occurs less commonly than in elderly adults, but its consequences can be equally devastating.
- Evaluation for causes and risk factors, short-term stroke treatments, rehabilitation, and long-term prevention of future strokes all play a very prominent role in stroke care for children and young adults.
- Optimal stroke care in young people requires multidisciplinary expertise, including specialists in blood clotting, neurology, radiology, rehabilitation, neuropsychology, and other areas.
- Thrombophilia testing is an important part of the evaluation of causes and risk factors for stroke in children and young adults, and is best guided by experts in blood clotting. Thrombophilia affects decision-making for both short-term treatment and long-term prevention of future strokes.
- Patients taking aspirin/blood thinners should exercise appropriate bleeding precautions. In addition, patients on aspirin therapy should receive annual flu shots, and should suspend aspirin use during illnesses (especially flu-like symptoms).
- Long-term management of ischemic arterial stroke is focused primarily upon safely preventing further strokes, as well as optimizing the child's/young adult's level of function in school, work, family, and/or society.

The use of aspirin during active influenza (i.e., flu) and perhaps other viral illnesses has been associated with a rare condition of liver failure, Reye's syndrome. For this reason, annual flu shots are essential in patients taking aspirin, and the use of aspirin should be suspended during times of illness (especially flu-like symptoms).

For non-urgent concerns relating to bleeding or aspirin/blood thinners, patients should contact their Hematologist or primary care physician.

OTHER PRACTICAL CONSIDERATIONS

It is important to work with a knowledgeable team of health care providers, including specialists from Hematology, Neurology, Radiology, and Rehabilitation, in the care of the child or young adult with ischemic stroke. Thorough evaluation of stroke is often challenging, and both short-term and long-term treatment decisions can be difficult. The identification of thrombophilia is an important component of this care, and is best guided by experts in blood clotting. Family testing should be considered for young stroke patients in whom genetically-determined thrombophilia traits are identified. A list of centers specialized in clotting disorders can be found on the web at www.nattinfo.org/provider.htm.

Radiologic imaging tests (scans)

Suspected stroke is confirmed by scans, typically magnetic resonance imaging (MRI) of the brain. Computed tomography (CT) of the brain is often also performed initially. In children who develop stroke after the first month of life, additional specialized scans of the blood vessels in the brain and neck are important to evaluate for abnormalities in the arteries (blood vessels that deliver blood) in these areas, including narrowing and blood clots.

Laboratory tests and other exams

Other steps in the evaluation include: laboratory testing for thrombophilia; laboratory screening for metabolic disorders (medical conditions caused by abnormalities in proteins called "enzymes" that control levels of important chemicals and nutrients in the blood or body tissues); and echocardiography (heart ultrasound) to evaluate for heart defects, valve disease, or blood clots in the heart that could cause thromboembolic stroke (a type of ischemic stroke due to blood clots from the venous system of the body that have traveled, or "embolized", to the arterial circulation of the brain, often suspected when more than one area of stroke is seen on the scans or in patients with thrombophilia. Genetic testing may be performed for certain metabolic disorders, especially in patients who have other medical conditions of unclear cause. In some cases, the evaluation may also include blood testing for

rheumatologic conditions and certain infections that are thought to cause stroke in young people.

WHAT THROMBOPHILIA TESTING SHOULD BE PERFORMED IN CHILDREN AND YOUNG ADULTS WITH ISCHEMIC STROKE?

Thrombophilia testing for stroke risk factors can vary across treatment centers. However, because thrombophilia is common in young stroke patients and may affect short- and long-term treatments, comprehensive thrombophilia testing recommended by a group of blood clotting experts, the Scientific Subcommittee on Perinatal and Pediatric Thrombosis of the International Society on Thrombosis and Haemostasis, is routinely performed at many specialty centers. This includes testing for: anticoagulant deficiencies (protein C activity, free protein S antigen, antithrombin activity); antiphospholipid antibodies (lupus anticoagulant, anti-beta-2-glycoprotein-I antibody, anti-cardiolipin antibody); elevated homocysteine concentration; factor V Leiden mutation; prothrombin 20210 mutation; elevated factor VIII activity; and elevated lipoprotein(a) concentration. Testing for methylene tetrahydrofolate reductase (MTHFR) mutations may also be considered. For nearly all of the above-mentioned factors, clinical studies have suggested an increased association with ischemic stroke in young people.

heart attacks in older adults.

Due to its effect on platelets, aspirin can increase the risk for bleeding, especially after injury. For this reason, patients taking aspirin who develop significant bleeding or become significantly injured should seek medical evaluation. Patients on aspirin or other blood thinners should always use proper safety restraints (e.g., seatbelt) in a motor vehicle and wear a helmet when on a bicycle, skateboard, rollerskates, etc. High-impact physical activities and contact sports should generally be avoided while on treatment doses of aspirin, given the risk of bleeding from injury. The risk for life-threatening bleeding in the brain in association with head injury is of particular concern while on aspirin/blood thinners.

In order to help assure the proper medical treatment during medical emergencies, patients who are on aspirin therapy should either wear a medical bracelet showing that they take aspirin, and/or carry a list of their medications in their wallet or purse at all times. Patients taking aspirin should advise their physician/surgeon of their aspirin use prior to undergoing surgery or other invasive medical procedures; typically, aspirin is discontinued ten days prior to these procedures. In addition, other medications that increase the risk for bleeding (e.g., ibuprofen, naproxen, certain herbal products) should be avoided while on aspirin therapy, unless prescribed and monitored by a physician.

and ultimately discontinued in the absence of further seizure difficulties. In many older children and young adults with seizures due to stroke, long-term use of seizure medications may be necessary.

Rehabilitation (“rehab”) and support

Enabling the child/young adult to function as best as possible in school, work, family, and/or society involves rehab evaluation and services (for example, physical and occupational therapies), neuropsychological assessment and services (counseling, adaptive educational tools, etc.), and Neurology follow-up (including seizure control and prevention, as well as examination for neurologic changes). Children and young adults with stroke who have thrombophilia are also followed by blood clotting specialists in Hematology (e.g., monitoring of blood thinners, evaluation and management of bleeding concerns, prevention of blood clots during times of increased risk for blood clot development, recommendations for other family members to consider testing for the thrombophilia).

HOW DOES ASPIRIN WORK, WHAT ARE ITS SIDE EFFECTS, AND WHAT PRECAUTIONS SHOULD BE TAKEN WHILE ON ASPIRIN?

Aspirin interferes with the function of blood clotting cells called platelets, and has been shown to decrease the risk of second strokes or

HOW IS ISCHEMIC STROKE IN CHILDREN AND YOUNG ADULTS INITIALLY TREATED?

The initial treatment of ischemic stroke in young people is complex, and is often different for patients with different circumstances. To date, other than in sickle cell disease patients, no clinical trials have been completed to guide the initial treatment of ischemic stroke in children and young adults. The initial treatment of ischemic stroke must emphasize to the safe medical control of blood pressure, seizures, fluid levels, and blood levels of oxygen, sugar, salts, acid, etc. Additional important treatment decisions involve consideration of the identified causes and risk factors for stroke, the amount and area of the brain affected, and the medical status of the patient.

In a child or young adult with recent stroke where blood flow to the brain continues to be decreased due to a narrowing or blood clot in an artery, anticoagulant (i.e., blood thinner) medicines such as heparin are often considered, particularly when the risk for bleeding is believed to be less than the possible benefit of preventing clot formation or growth (and in this way preventing further stroke). In other patients, aspirin is used to prevent further stroke. In newborn infants with stroke, usually no blood thinner or aspirin therapy is recommended, unless strong thrombophilia has been shown in the laboratory testing.

In rare cases of stroke diagnosed within the first several hours of the onset of signs/symptoms, special treatments and techniques to remove or break up a blood clot, called thrombolysis, may be possible. In older adults who are being treated within the first three hours of the onset of signs/symptoms of stroke, the intravenous (I.V.) administration of a thrombolysis medication called tissue-type plasminogen activator (tPA) has been shown to be safe and effective in decreasing the negative outcomes of stroke when patients are carefully selected. Although the safety and possible benefit of these approaches in children and young adults have not yet been thoroughly studied, there are reported cases in which they have been used effectively.

HOW IS ISCHEMIC STROKE IN CHILDREN AND YOUNG ADULTS TREATED OVER THE LONG-TERM?

Long-term management of ischemic arterial stroke is focused primarily upon: (1) safely preventing further strokes; and (2) enabling the child/young adult to function as best as possible in school, work, family, and/or society.

Prevention

In an effort to prevent future strokes, most children and young adults who have a history of ischemic arterial stroke that occurred after the neonatal period are maintained on daily aspirin.

The dose typically chosen is for initial treatment is 3-5 mg/kg orally each day; often a lower dose of approximately 2 mg/kg is chosen for long-term treatment. Some patients, such as those with antiphospholipid antibody syndrome (i.e., whose thrombophilia testing showed lasting antiphospholipid antibodies in the blood since the time of stroke), those with ongoing vessel abnormalities, and individuals who have had further stroke while on adequate aspirin treatment, may also be prescribed long-term blood thinners, such as warfarin (Coumadin®).

In patients with certain underlying medical conditions, other treatments aimed at improving the underlying disorder may also decrease the risk of further stroke. For example, in patients with cholesterol abnormalities, cholesterol-lowering medicines may also be given, and in patients with rheumatologic conditions, drugs to control the overactive immune system may also be used.

Seizure control

Depending upon the area(s) of the brain affected, seizures are often a concern in patients with stroke. In some cases, such as stroke in newborn infants, seizure may be the main sign of a stroke.

A variety of medications are available to control seizures in young patients with stroke. In newborns, phenobarbital is frequently used, and often can be weaned over weeks to months